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LETTER

Response to Article "Ultrasensitive Hierarchical AuNRs@SiO_2@Ag SERS Probes for Enrichment and Detection of Insulin and C-Peptide in Serum" [Letter]

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Dear editor

It is my great pleasure to express my interest in a thorough and insightful review on the recently published research article "Ultrasensitive Hierarchical AuNRs@SiO_2@Ag SERS Probes for Enrichment and Detection of Insulin and C-Peptide in Serum" written by Zhang et al.[1] This research focuses on the simultaneous identification of the diabetes biomarkers C-peptide and insulin in human serum using highly sensitive Surface-Enhanced Raman Spectroscopy (SERS). Diabetes mellitus is a chronic endocrine and metabolic disorder and is a major global health issue. Maintaining blood glucose levels within a healthy range is essential for effective diabetes management to prevent complications, such as kidney failure, blindness, cardiovascular disease, and neuropathy. Insulin biosensors are an ideal tool for monitoring glucose levels, physical activity, dietary management, and the use of antidiabetic drugs.[2] Along with insulin levels, assessments of insulin secretory capacity are valuable for classifying different forms of diabetes, stratifying patients at risk for complications, and guiding treatment choices. C-peptide secretion has become an important clinical marker, particularly in autoimmune diabetes and especially in adult-onset diabetes, as it reflects beta-cell function.[3]

In this research, authors developed a nanomaterial-mediated sandwich SERS biosensor for the simultaneous detection of insulin and C-peptide. Gold nanorods@Ramantags@SiO_2@Ag nanocomposite was prepared by a series of surface functionalization through chemical reaction. Amine-modified nanorods@Ramantags@SiO_2@Ag was added with $AgNO_3$ to form the SERS complex (Au@Ramantags@SiO_2@Ag). Antibodies (Insulin or C peptide) were further attached with the SERS complex through the interaction of amine. To make a sandwich assay, the antibody (Insulin or C peptide) was conjugated with carboxylated magnetic bead and then interacted with an antigen. This antibody-antigen conjugation was sandwiched with SERS complex to get the SERS signal. The authors incorporated Ag nanoparticles on SiO_2 to form a core-shell satellite structure, which improves the SERS performances and detects C-peptide and insulin. Furthermore, the newly developed SERS probe detects C-peptide and insulin from the diluted human serum as low as 1.76×10^{-10} nM, and 4.29×10^{-5} pM, respectively.

This SERS approach presents a new viewpoint in the area of diabetic sensing and has a great deal of potential for the quantitative detection of a wide range disease-related biological markers. At the same time, the authors displayed the drawback of the proposed strategy in reproducibility and aggregation of nanomaterials, in addition a potential possibility of nonspecific target binding. To make an improvement towards non-biofouling, the authors need to consider the blocking agent for surface functionalization in this research. Bovine serum albumin (BSA) was used as the blocking molecule to reduce the biofouling after antibody attachment on the Au@Ramantags@SiO_2@Ag and carboxylate magnetic bead. In the surface functionalization, (3-Aminopropyl)triethoxysilane was used as a chemical-linker to attach

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antibody and then BSA was added. In principle, BSA cannot cover the excess amine surface completely. At the same time various research proved that excess amine surfaces easily attract other biomolecules non-specifically and lead to the false positive result.[4] I suggest authors to consider other blocking agent, such as polyethylene glycol-based polymers that can effectively cover the excess surfaces on the SERS complex in order to reduce the biofouling, improve the nanoparticle stability, and enhance the efficacy on detecting glucose and C-peptide.[5] Overall, this research methodology is attractive as a diabetes sensor, and this biosensor might be effective for detecting other biomolecules and diagnosing diseases at early stages. Additionally, similar sensing strategies could be developed to offer new possibilities for point-of-care and high-performance testing.

Disclosure

The authors report no conflicts of interest in this communication.

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